REMARKS

Claims 1-4 and 10-22 are pending. Claims 1, 10 and 18 have been amended.

Support for amended claims 1 and 10 may be found in original claims 1 and 10, respectively. Support for the amendment of claim 18 may be found on page 2, lines 32-34; page 28, lines 19-29; and in original claim 18. Applicants maintain that the amendments do not raise an issue of new matter. Entry of this Amendment is respectfully requested.

The claims were objected to as not being numbered in accordance with 37 CFR 1.126. The January 20, 2006 Preliminary Amendment purported to cancel all claims except for claims 1-4 and 9-22. Nevertheless the January 20, 2006 Claim Listing did not indicate the status of claim 9. The undersigned apologizes for the resulting confusion. Claim 9 should have been canceled, and in the Claim Listing submitted herewith claim 9 is listed as canceled. It is believed that the claim objection has been overcome.

1. INVENTION IS ENABLED

(A) HETEROAROMATIC

Claims 1-4 and 10-22 have been rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the heteroaromatic ring-containing compounds allegedly are not adequately enabled. The rejection is respectfully traversed.

The claims have been amended to delete "5- or 6-membered heteroaromatic ring . . ." from the recited definition of variable "A" in Formula I. Accordingly this ground of rejection is now moot and should be withdrawn.

(B) TREATMENT OF LISTED DISEASES

Claims 10-22 have been rejected under 35 U.S.C. § 112, first paragraph, on the grounds that "the specification, while being enabling for reducing glucose, triglycerides and free fatty acids in C57BL/Ksola mice it does not reasonably provide enablement for treating all insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis, and arteriosclerosis." (March 18, 2009 Office Action, pages 5-6).

(1) Pharmaceutical composition claims don't list diseases

Claims 18-22 are directed to a pharmaceutical composition. None of claims 18-22 recites a disease or a list of diseases. Accordingly, the claims are not limited by a recited use.

The rejection acknowledges that the specification is "enabling for reducing glucose, triglycerides and free fatty acids in C57BL/Ksola mice. . . ." (March 18, 2009 Office Action, page 5). Thus the Office accepts that there is an enabled use.

"[W]hen a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use." MPEP § 2164.01(c), Rev. 7, July 2008, page 2100-195, right column, last paragraph. See also *In re Brana*, 51 F.3d 1560, 34 USPQ.2d 1436 (Fed. Cir. 1995); *Cross v. Iizuka*, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); *Application of Krimmel*, 48 CCPA 1116, 292 F.2d 948, 130 USPQ 215 (1961).

This rejection is based on the position that the specification "does not reasonably provide enablement for treating all insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and

arteriosclerosis". (March 18, 2009 Office Action, pages 5-6). But claims 18-22 are not limited by a recited use and it is undisputed that the specification provides an enabled use. Therefore a rejection for nonenablement is improper.

(2) Methods of treatment are enabled.

The rejection is also improper with regard to claims 10-17, which do recite the treatment of certain diseases. The Office bears the burden of establishing that an invention does not satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph. As stated by the CCPA in *In re Marzocchi*:

> "As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support."

(*In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, ___) (underlining added). It is not sufficient for the Office to simply assert that it doubts the correctness of the statements in the disclosure. The Office must back up its doubts with evidence or reasoning. Again from *Marzocchi*:

> "In any event, it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement."

(*Id.* at 224) (internal citations omitted) (underlining added).

The rejection has cited the alleged unpredictability of the pharmaceutical arts in general. The rejection stated:

> "e) The state of the clinical arts in treating or preventing diseases is unpredictable. . . . g) It is well established that 'the scope of enablement varies inversely with the degree of unpredictability of the factors involved', and physiological activity is generally considered to be an unpredictable factor."

(March 18, 2009 Office Action, page 7) (citations omitted). But that does not constitute adequate reasoning to support an enablement rejection. If the mere assertion that the chemical, pharmacological and medical arts are unpredictable would be accepted as sufficient reasoning, it would mean that in the case of all chemical, pharmacological and medical inventions applicants would have the burden of demonstrating enablement rather than the Office having the burden of demonstrating that an invention is not enabled. And that would be contrary to the law as articulated in *Marzocchi* above.

The rejection states, "The scope of the claims involves all of the thousands of compounds of claim 1 as well as the hundred[s] of diseases embraced by the term anti-tumor and anti-virus. Thus, the scope of the claims is very broad." (March 18, 2009 Office Action, page 8). First, characterizing something as broad is not a reason to doubt that the invention works as claimed. Second, assuming for the sake of argument that the breadth of claim scope were relevant to the enablement inquiry, it is clear that no reliable estimation of the claim scope can be made if the claims are mischaracterized. Applicants take no position on the number of diseases embraced by the terms anti-tumor and anti-virus. But it is unclear why the number of diseases embraced by the terms anti-tumor and anti-virus is supposed to be probative of the scope of the claims pending in this application, which do not recite the treatment of tumors or viral infections.

The specification describes how to make the recited compounds, how and in what amounts to administer them, and for the treatment of what conditions. No

adequate reason has been given to doubt that the invention works as claimed, without undue further experimentation. Contrary to the position of the rejection, clinical trials are not required to enable a method of treatment invention.

In view of the guidance provided in the specification, applicants respectfully submit that the person of ordinary skill in the art would not have doubted that the claimed compounds are useful in the recited therapies and would not have required undue experimentation to practice the claimed invention.

2. NO OBVIOUSNESS-TYPE DOUBLE PATENTING

Claims 10-22 have been provisionally rejected on grounds of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-5, 7, 9-11 and 67 of cpending Application No. 11/535,779 and over claims 1-7, 9-12 and 14 of copending Application No. 11/841,508. The double patenting rejections are respectfully traversed.

The rejection stated that the allegedly "conflicting claims . . . are not patentably distinct from each other because they differ only in the chalcogen use in the linking group, oxygen vs. sulfur. The use of one chalcogen in lieu of another would have been obvious to [o]ne of ordinary skill in the art as such could be readily envisaged and the results would not have been unexpected." (March 18, 2009 Office Action, page 9).

The person of skill in the art would not have had a reasonable expectation that exchanging sulfur for oxygen in the allegedly conflicting claims would yield compounds having the same or similar activity. It is well known in the art that the biological activities of thio- and oxygen-containing analogs can have significantly different biological activities.

Shinkai, et al. (J. Med. Chem. (2000) 43: 3566-3572) (of record) reports on the cholesteryl ester transfer protein (CETP) inhibitory activity in human plasma of a series of compounds. Table 2 (page 3569) shows the structures and IC_{50} of compounds 14 and 15. Compounds 14 and 15 are structurally identical except that one oxygen molecule of compound 15 is replaced by sulfur in compound 14. Shinkai reports that "the thioester **14** . . . showed activity. . . . Since the ester **15** did not show activity, the sulfur atom was essential." (page 3568, left column, last six lines). In this case the sulfur-containing compound was active and its oxygen-containing analog was inactive.

In view of the knowledge in the art that oxygen and sulfur analogs can have significantly different biological activities, the person of skill in the art would not have been able to predict with a reasonable degree of confidence that the compounds of the instant invention would have the same or similar activities as the compounds claimed in the '779 application or the '508 application.

Applicants respectfully submit that the double patenting rejections have been overcome.

3. CONCLUSION

In view of the amendments and the preceding remarks, applicants respectfully submit that the subject application is now in condition for allowance. Reconsideration and withdrawal of all rejections and objections, and prompt notice of allowance, are respectfully requested.

No fee is believed necessary in connection with the filing of this Amendment. If any fee is required, the Commissioner is hereby authorized to charge the amount of such fee, or to refund any overpayment, to Deposit Account No. 50-1677.

Respectfully submitted,

/Lewis J. Kreisler/

_____

Lewis J. Kreisler
Reg. No. 38522
Attorney for Applicant(s)

930 Clopper Road
Gaithersburg, MD 20878
Phone: (240) 631-2500 x3276
Facsimile: (240) 683-3794